REMARKS

Claims 1, 5, and 7-28 are pending and claims 1 and 7-13 are currently under examination. Claims 5 and 14-28 are withdrawn. Claims 2-4 and 6 have been previously canceled. No new matter is added. Reconsideration of the pending claims is respectfully requested.

Priority

The Examiner assets that the claimed invention dos not receive benefit to the February 13, 2004 or February 27, 2004 provisional applications. Applicant respectfully traverses this rejection.

The Examiner stated that not all of the SNPs provided in Table 2, as now claimed, are presented in the provisional applications. Applicant respectfully disagrees. Claim 1 is limited to the sequences listed in Table 2. SEQ ID NOs: 1-9, 42-43 and 46-48 are disclosed in both provisional applications: 60/544,788 filed February 13, 2004 and 60/548,370 filed February 27, 2004. In addition, SEQ ID NOs: 27, 29-31, 40-41 and 45 are disclosed in the Frudakis 2003 article (Frudakis *et al.*, 2003, Genetics 165:2071-2083), which is incorporated by reference in the provisional application 60/548,370 filed February 27, 2004. (See paragraph [0049] on page 17 of 60/548,370). Additionally, Applicant identified the SNPs associated with eye color using a commercially available gene chip (GeneChip© Mapping 10K Array and Array Set from Affymetrix). (See paragraph [0051] on page 21). This gene chip and its contents were publically available at the time of filing of both provisional applications. Therefore, at the time of filing the provisional applications, 60/544,788 and 60/548,370, the SNPs on the gene chip were in the public domain. Applicant submits that the pending claims are entitled to the priority of both provisional applications 60/544,788 filed February 13, 2004 and 60/548,370 filed February 27, 2004.

The Examiner stated that though the elected SNPs SEQ ID NO:3 and SEQ ID NO:4, rs1004611 and rs1874835, are mentioned in the provisional applications, neither of the disclosures teach how to infer an eye color based upon an allele.

Applicant respectfully disagrees. Example 2 and Table 2 of the provisional application 60/548,370 filed February 27, 2004 disclose a set of 35 SNPs. This same set of SNPs is also disclosed in the provisional application 60/544,788 filed February 13, 2004. Applicant submits that the disclosure of a set of 30-40 SNPs associated with human eye color provide sufficient guidance to those skilled in the art. Applicant started from a total of 10,000 SNPs using a commercially available gene chip. (See paragraph [0051] on page 21). Accordingly, Applicant presented novel and groundbreaking work by narrowing down the number of SNPs and associating the SNPs with a phenotype. The gene chip used by Applicant was publically available at the time of filing of both provisional applications. Using the disclosure provided in the provisional applications, one skilled in the art could easily have detected the relevant SNPs and from that information inferred eye color. As such, one skilled in the art would be able to make and use the invention as disclosed in the provisional applications. Applicant submits that the pending claims are entitled to the priority of both provisional applications 60/544,788 filed February 13, 2004 and 60/548,370 filed February 27, 2004.

Claim Rejections – 35 USC § 112 - First Paragraph

Claims 1 and 7-13 remain rejected under 35 U.S. C. 112, first paragraph, for lack of enablement. Applicant respectfully traverses this rejection.

First, the Examiner states the following for unpredictability:

> "While the state of the art and level of skill in the are with regard to the detection of any known polymorphic allele is high, the level of unpredictability in associating any particular allele with a specific phenotype is even higher. The high level of unpredictability is demonstrated by the prior art, the post filing art, and the instant specification."
>
> Page 6, lines 12-15 of the Office Action dated May 27, 2011

Applicant respectfully disagrees. While the state of the art and level of skill is high for the identification of new SNPs or the association of SNPs with a particular phenotype, the state of the art and skill level for detecting a known SNP is not high. Since the late 1990s, when gene chip technology was first introduced, the technology and skill required to detect

SNPs has significantly lessened. All one of skill in the art must do to detect a SNP is to obtain a sample and use the commercially available gene chips to detect the SNPs present in the sample, all of which is considered routine lab work in most laboratories. The reproducibility of detecting SNPs is considered as good as other routine lab procedures, such as DNA sequencing.

The Examiner has stated that the specification does not support the assertion that these SNPs are statistically significant. Applicant disagrees. The association of a particular SNP pattern with a specific phenotype requires high skill. As argued previously, Applicant has narrowed the list of 10,000 SNPs to 32 that are associated with eye color. These SNPs were derived from 10,000 known SNPs, using 800 samples. Additionally, the SNPs were selected using several statistical methods: delta number, Pearson's P value or Odds ratio test. These examiner further stated:

> The specification acknowledges that a differential of 10% would be significant with a sample of 500 or so at the 0.05 level but not with a sample of 100. Here the delta value for SEQ ID NO: 3 and 4 is 2% and 11 % respectively (see Table 3, page 26). Moreover, the sample size was much less than 100 (21 light and 21 dark eye colored samples) which the specification clearly states a 10% delta would not be significant with a sample of 100.
>
> Page 11, lines 10-15 of the Office Action dated May 27, 2011

However, the Examiner has not considered that the specification goes on to say:

> "Since the interest was in confirming the original data, the p-value can be misleading because the sample sizes are unequal; the allele frequency differential is a better parameter to use. Most of the differentials were similar, showing good reproduction, even though p-values for most of these differentials in a sample of 100 was not significant at the 0.05 level (many were close). The differences in delta value from the first 800 and the second 100 can be due to sample size effects, or because the eye colors were measured more objectively with a camera for the second 100."
>
> Page 8, paragraph [0061] 10/589,291 specification

Applicant submits that based on the above arguments and statements that the predictability of detecting SNPs is much higher than asserted by the Examiner, the state of the art and skill level required are lower than the Examiner asserted and that the invention is statistically sound.

Second, the Examiner states the following for guidance of experimentation:

> "Moreover, it is unclear how the skilled artisan would infer eye color in the event ALL SNPs "were not correct". For example, if nucleotide 68 of SEQ ID NO:3 were to indicate a darker eye shade and nucleotide 171 of SEQ ID NO:4 were to indicate a lighter eye shade. There would be no reason inference to be made. Stated another way, it is unpredictable how one would infer natural eye color in half of the SNPs indicated dark eye color and the other half of the SNPs indicated light eye color.
>
> Furthermore, it is unclear how one would infer natural eye color. Rebbeck teaches 7 categories of eye colors, namely blue, gray, green , hazel, light brown, dark and black. The specification only analyzes two categories: dark or light.
>
> This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps."
>
> Page 9, line 17- Page 10, line 3 of Office Action dated May 27, 2011

The Federal Circuit has held that "[t]he enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998) (citing *Engel Indus., Inc. V. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991); *see also Invitrogen Corp. v. Clontech Laboratories, Inc.*, 429 F.3d 1052, 1071 (Fed. Cir. 2005). Thus, Applicant submits that the claimed invention is fully enabled because the specification provides sufficient guidance with significant experimental procedures and data.

Further, the Federal Circuit has held that routine experimentation does not constitute undue experimentation, stating that:

> "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the

> determination of how to practice a desired embodiment of the invention claimed." (citation omitted).
>
> *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996)

The Federal Circuit has elaborated on the gap-filling principle, stating:

> "That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art."
>
> *AK Steel Co. v. Sollac*, 344 F.3d 1234, 1244.

Applicant respectfully traverses the Examiner's assertions. Applicant submits that under the enablement standards set out above not every permutation of the invention must be specifically set out in the specification for the invention to be enabled. Rather, an invention is enabled if it describes any mode of making and using the invention. Applicant asserts that the disclosure of the present invention is more than adequately enabled. Example 1 describes in detail now to make and use the invention. Paragraphs [0010]-[0012] describe in detail the process of identifying a SNP and associating SNP patterns with an eye color. Additionally, paragraph [0015] describes how the identified SNPs are compared with a database containing known SNPs related to eye color. While not every possible variance is disclosed, one skilled in the art would be able to detect the SNPs associated with eye color.

Applicant wishes to clarify that obtaining the SNPs alone does not predict human eye colors. The obtained SNPs are compared to known sequences where eye colors are previously known. For example, paragraph [0059] on page 26 of the specification states the following:

> [0059] The iris color of a subject can be predicted from a nucleic acid sample by determining the genotype of the sample with respect to SNPs as shown in Table 2 (e.g., with one or more of the SNPs of SEQ ID NOS: 1 to 7); comparing the genotype against those for known subjects in a database (*i.e.*, subjects for whom eye color has been associated with nucleotide

> occurrence(s) of the SNPs; and identifying known subjects whose genotypes match the unknown sample. The iris colors of the known subjects thus provide a guide.

Accordingly, there should not be a "fictional combination" of selected SNPs as asserted by the Examiner such as "all SNPs were not correct." Applicant submits that most of human sequences of selected SNPs have relatively common patterns for inferring human eye colors, and that is the reason why the method of the claimed invention is robust for a majority of cases tested. Thus, the specification provides sufficient guidance and only routine experimentation is needed to carry out the claimed invention.

Applicant also wishes to clarify that the disclosure of the specification is not limited to two categories of human eye colors as asserted by the Examiner. In fact, various classification systems can work well based on the disclosure of the specification. For example, paragraphs [0064]-[0066] on page 28 of the specification provides a classification model with five classes, where human eye colors are classified from class 1 to class 5. Applicant submits that the claimed invention recites two categories of human eye colors for accommodating self-reporting colors in the samples tested. For example, a particular individual may have scientifically green eyes but prefer to self-report as blue eyes. Thus, categorizing this individual as a light eye color can avoid such dilemma.

Third, the Examiner states that Table 2 does not provide any data for human eye colors, stating that:

> "The response further relies upon Table 2, however, Table 2 does not appear to provide any data of eye shade/alleles. Table 3 provides 10 SNPs and their delta and gene and allele/eye shade, but for the reasons discussed above, there is no significant association that the skilled artisan may reasonable infer natural eye color. It is unclear what the ordinary artisan would infer if SEQ ID NO: 3 was a T and SEQ ID NO: 4 was a G.
>
> The response relies upon Exhibit A, but as discussed above, Exhibit A fails to address each of the SNPs in Table 2 and fails to provide how to infer based upon the SNPs provided in the reference."
>
> Page 12, lines 9-19 of the Office Action dated May 27, 2011

Applicant wishes to clarify again that the sequences of SNPs listed in Table 2 or Table 3 alone do not infer human eye colors. As discussed above, the inferring process relies on the associations between patterns of SNPs and samples of known eye colors. The pending claim 1 has a three-step process and the identifying SNPs step alone does not automatically infer an individual's eye color because the comparing step is needed to examine SNP patterns with samples of known eye colors. Further, claim 1 requires the identification of all of the SNPs in Table 2, but only the association of the SNPs in SEQ ID NOs:1-9 with an eye color. Paragraphs [0010]-[0012] describe in detail the process of identifying a SNP and associating SNP patterns with an eye color. Additionally, paragraph [0015] describes how the identified SNPs are compared with a database containing SNPs known to be related to eye color. Example 1 also describes in detail how to make and use the invention. Accordingly, the specification provides sufficient guidance to those skilled in the art regardless the presence or absence of eye color data in Table 2.

In summary, Applicant submits that the claimed invention is fully enabled because specification provides sufficient disclosure for one skilled in the art to make and use the claimed invention. Applicant has accomplished the major groundbreaking work to rule out more than 9,900 SNPs and narrows down to a set of 30-40 statistically significant SNPs for inferring eye colors. The state of the art and skill level required to practice the invention is not high as asserted by the Examiner, as detecting SNPs is a routine procedure for one skilled in the art and Applicant has discloses the association of SNPs with eye color. The specification has provided sufficient guidance for those skilled in the art to detect the relevant SNPs and associate the resulting SNP pattern with eye color. Thus, withdrawal of the lack of enablement rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and the remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this case.

Please charge Deposit Account 07-1896 in the amount of $465.00 to cover a Request for Continued Examination fee and $280.00 for a Petition for a Two Month Extension of Time fee. No additional fee is deemed necessary with the filing of these papers. However, in any event that any additional fee is due, the Commissioner is hereby authorized to charge any fees required by this submission, or make any credits or overpayments, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

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Lisa A. Haile, J.D., Ph.D.
Registration No.: 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER LLP (US)
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO Customer No.: 28213